Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 16-42, 44-47, 50, 51, 53 and 57-77 are pending in the application. Claims 43 and 78 have been canceled without prejudice or disclaimer. Applicants retain the right to pursue the subject matter of the canceled claims in one or more continuing applications. Claims 44-48, 50-51, 53, 57-59, 71-72, and 76-77 have been amended in order to more clearly and precisely define the subject matter of the invention. Support for the amendment can be found throughout the specification and original claims. For example, support for the amendments can be found in the specification at page 14, lines 27-28; page 18, lines 3-29; and page 24, lines 14-17. The amendments add no new matter. Thus, entry of the amendments is respectfully requested.

Claims 16-42 have been allowed.

Claims 43-47, 50, 51, 53, and 57-78 stand rejected.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Interview with the Examiner

Applicants thank Examiner Karen Canella for the courtesy extended in the personal interview held on May 6, 2002. Applicants respectfully request that Examiner Canella forward an interview summary at her earliest convenience.

Claims Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 44-45, and 57-77 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that Applicants, at the time the application was filed, had possession of the claimed invention. (Paper No. 26, page 2.) Applicants respectfully disagree and traverse the rejection.

The Examiner has stated that "[w]ith the exception of degenerate coding sequences as applied to SEQ ID NO:1, the specification does not give examples of defined polynucleotide variants or defined variants of SEQ ID NO:2 that would have the same function as the disclosed SEQ ID NO:1 or SEQ ID NO:2." (Paper No. 26, page 4.) The Examiner has also provided references which allegedly support the assertion that "[t]he substitution or deletion of amino acid residues to make a variant protein is probably one of the most unpredictable areas of biotechnology." (*Id.*) In addition, the Examiner has stated that "it could not be predicted that a variant polynucleotice. . .would function as suggested and the specification provides nor [sic] guidance on how to use these variant polynucleotides." (*Id.*) As evidenced from these comments, the Examiner appears to be suggesting that the alleged difficulties in predicting whether or not a variant BCSG-1 polynucleotide has retained the biological activity and/or function of BCSG-1 and the alleged failure of the specification to provide examples of functional variants speaks to the issue of whether or not the claims meet the written description requirement.

Applicants respectfully submit that the issue the Examiner raises is not relevant to the written description requirement. This is because the claimed polynucleotides need not encode *fully functional* BCSG-1 polypeptides in order to have a "function" to be used in the context of the claimed invention. For example, the specification teaches that BCSG-1 can be used as a breast cancer progression marker. (Page 51, lines 1-2.) In this use, isolated BCSG-1 polynucleotides and fragments and variants thereof, may be used to detect the expression levels of BCSG-1 in patients using methods such as Northern blots and PCR. (Specification, page 29, lines 8-16.) Also, BCSG-1 polynucleotides and fragments and variants thereof, may be used to generate BCSG-1 specific antibodies which may be used in immunoassays for the detection of BCSG-1 protein levels in patients. (Specification, page 29, lines 17-21.) All such methods are described in the specification and do not require the variant polynucleotide to encode a *fully* functional BCSG-1 protein. Rather, the isolated variant polynucleotide, for example, need only be capable of hybridizing to BCSG-1 from a patient (as in Northern blot methods) or encoding a protein with an antigenic region capable of generating BCSG-1 specific antibodies (for use in immunoassays) to be considered useful. To that end, Applicants have taught the complete nucleotide sequence of BCSG-1, methods for isolating BCSG-1, and predicted antigenic regions of BCSG-1.

Accordingly, Applicants submit that whether the claimed polynucleotides encode fully functional BCSG-1 proteins is not relevant to the issue of whether or not the claims find adequate written description in the specification.

Claims 44-45 and 57-59

Claims 44-45 and 57-59 have been amended. As amended, claims 44-45 are directed to polynucleotides *consisting of* at least 100 contiguous nucleotides of the coding region of SEQ ID NO:1, or the complement thereof, or polynucleotides *consisting of* at least 250 contiguous nucleotides of the coding region of SEQ ID NO:1, or the complement thereof. Claims 57-59 are directed to polynucleotides which encode a polypeptide *consisting of* at least amino acids 94 to 107 of SEQ ID NO:2 or polynucleotides which encode a polypeptide *consisting of* at least amino acids 120 to 127 of SEQ ID NO:2. These claims find adequate written description in the specification and satisfy the requirements of 35 U.S.C. § 112, first paragraph.

The written description requirement is met if the patent specification describes the invention "in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claim invention'." *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir.), *reh'g, en banc, denied*, 1997 U.S. App. LEXIS 31640 (Fed. Cir. 1997), *and cert. denied*, 523 U.S. 1089, 140 L. Ed. 695, 118 S. Ct. 1548 (1998). In *Eli Lilly & Co.*, the Federal Circuit squarely dealt with the issue of written description for claims directed to genetic material. In order to satisfy the written description requirement, the court held that:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

(*Id.* at 1569.) The court emphasized that the written description must provide structural features common to the members of the genus which would allow one of ordinary skill in the art to "visualize or recognize the identity of the members of the genus." (*Eli Lilly & Co.*, 118 F.3d at 1568.) Thus, the standard to be utilized in determining whether or not the

written description requirement has been satisfied is whether one of ordinary skill in the art can "visualize or recognize" the members of the genus based on Applicants' disclosure.

The specification teaches that the invention is directed to fragments of isolated nucleic acid molecules having the nucleotide sequence of SEQ ID NO:1. (Page 8, lines 14-17.) Specific fragment lengths of 100 nucleotides and 250 nucleotide are described in the specification. (*Id.* at line 21.) The specification also teaches that the invention is directed to specific fragments encoding amino acids 94 to 107 of SEQ ID NO:2 and amino acids 120 to 127 of SEQ ID NO:2. (Page 9, lines 1-4.) SEQ ID NOs:1 and 2, located in the Sequence Listing and in Figure 1, provide the complete nucleotide sequence and amino acid sequence of BCSG-1, respectively. Applicants submit that this written description fully sets forth the claimed invention so that one of ordinary skill in the art could reasonably "visualize or recognize" the members of the genus.

Specifically, the structural features common to the members of the genus which would allow one of ordinary skill in the art to "visualize or recognize the identity of the members of the genus" are provided in SEQ ID NO:1 and/or SEQ ID NO:2. (*Eli Lilly & Co.*, 119 F.3d at 1559.) This is because SEQ ID NOs:1 and 2 provide the critical sequences that allow one of ordinary skill in the art to identify the polynucleotides encompassed by claims 44-45 and 57-59.

In view of the above, Applicants assert that the claims 44-45 and 57-59, and the associated dependent claims, are adequately supported by the specification. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claims 71, 72, 76, and 77

Claims 71, 76 and 77 are directed to percent identity variants ("at least 95% identical" at either the nucleotide or encoded amino acid level) of the BCSG-1 polynucleotide. SEQ ID NO:1 and SEQ ID NO:2 provide the polynucleotide and amino acid sequence of BCSG-1, respectively. SEQ ID NO:1 and SEQ ID NO:2 disclose sequences which are species of the genus of polynucleotides that are at least 95% identical to the BCSG-1 gene and polynucleotides which encode amino acid sequence that are at least 95% identical to the BCSG-1 protein. Thus, at least one member of the genus of polynucleotides encompassed by claim 71, 76 and 77 is disclosed.

According to the USPTO's own written description guidelines, the disclosure of "a single species may . . . provide an adequate written description of a generic claim when the description of the species would evidence to one of ordinary skill in the art that the invention includes the genus" and when the species that are described are "representative of the entire genus." (Federal Register, Vol. 66 No. 4, page 1102, 1106). Applicants submit that SEQ ID NOs:1 and 2, together with the added requirement that the polynucleotide encodes a polypeptide which binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 127 of SEQ ID NO:2, are representative of the genus of polynucleotides encompassed by claims 71, 76 and 77 and provide sufficient structural information to allow one of ordinary skill in the art to "visualize or recognize" the claimed invention.

One skilled in the art would be able to "visualize or recognize" innumerable members of the genus given the disclosure of SEQ ID NOs:1 and 2. Thus, Applicants assert that claims 71, 76 and 77, and the associated dependent claims, find adequate written description in the specification. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim 72 is directed to isolated BCSG-1 polynucleotides, which except for one to thirty conservative amino acid substitutions, encode an amino acid sequence selected from the group consisting of (a) amino acids 1 to 127 of SEQ ID NO:2; (b) amino acids 2 to 127 of SEQ ID NO:2; and (c) the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97856.

Applicants assert that provided with the nucleotide and amino acid sequence of BCSG-1 and Table 1, on page 21, which provides examples of conservative amino acid substitutions, one of ordinary skill in the art would be able to visualize or recognize the identity of the members of the genus. Accordingly, claim 72, and the associated dependent claims, finds adequate written description in the specification. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

Claims Rejections Under 35 U.S.C. § 102 and 35 U.S.C. § 103

The Examiner has rejected claims 43, 46, 50, 53, and 78 under 35 U.S.C. §102(b) as allegedly being anticipated by Adams *et al.* (WO 93/16178) as evidenced by Accession No. AAQ61421. (Paper No. 26, page 6.) Applicants respectfully traverse the rejection.

Solely to advance prosecution and not in acquiescence to the Examiner's rejection, claims 43 and 78 have been canceled and claims 46, 50 and 53 have been amended to recite an isolated polynucleotide consisting of at least 100 contiguous nucleotides of the coding region of SEQ ID NO:1 or the complement thereof or an isolated polynucleotide consisting of at least 250 contiguous nucleotides of the coding region of SEQ ID NO:1 or the complement thereof. Adams *et al.* allegedly disclose 80 contiguous nucleotides of SEQ ID NO:1. Thus, Adams *et al.* do not teach or suggest the subject matter of amended claims 46, 50 and 53. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also rejected claims 43, 46, 47, 50, 51, 53 and 78 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Adams *et al.* (WO 93/16178) in view of Sambrook *et al.* (Molecular Cloning, A. Laboratory Manual, 2nd Edition 1989, pages 10.27-10.28). (Paper No. 26, page 7.)

As discussed above, claims 43 and 78 have been canceled. Further, claim 44 from which claims 46, 47, 50, 51 and 53 depend, requires a polynucleotide consisting of at least 100 contiguous nucleotides of SEQ ID NO:1. Applicants submit, that Adams, taken alone or in combination with Sambrook *et al.*, does not teach or suggest polynucleotides consisting of at least 100 contiguous nucleotides of SEQ ID NO:1. As such, Applicants respectfully request withdrawal of this rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

The application is sought to be amended as follows:

In the Specification:

The paragraph beginning at page 1, lines 2:

The present application [is a Continuation-in-Part of Application Number 08/673,284 filed on June 28, 1996, which is herein incorporated by reference; said 08/673,284 claims the benefit of the filing date of provisional application 60/000,602, filed on June 30, 1995, which is herein incorporated by reference; the present application also] claims the benefit [to the filing date] of provisional application 60/037,080, filed February 3, 1997, which is [also] herein incorporated by reference.

In the Claims:

Claims 43 and 78 are canceled.

44. (Once amended) An isolated polynucleotide [The isolated polynucleotide of claim 43, comprising] consisting of at least 100 contiguous nucleotides of the coding region of SEQ ID NO:1 or the complement thereof.

45. (Once amended) The isolated polynucleotide of claim 44, [comprising] consisting of at least 250 contiguous nucleotides of the coding region of SEQ ID NO:1 or the complement thereof.

46. (Once amended) The isolated polynucleotide of claim [43] 44, which is DNA.

47. (Once amended) The isolated polynucleotide of claim [43] 44, which is RNA.

48. (Once amended) The polynucleotide of claim 44,[further comprising] linked to a heterologous polynucleotide.

50. (Once amended) A method of producing a vector that comprises inserting the isolated polynucleotide of claim [43] 44 into a vector.

51. (Once amended) A vector comprising the isolated polynucleotide of claim [43] 44.

53. (Once amended) A host cell comprising the isolated polynucleotide of claim [43] 44.

57. (Once amended) An isolated polynucleotide, encoding a polypeptide [comprising a nucleic acid which encodes an amino acid sequence] selected from the group consisting of:

(a) a polypeptide consisting of at least amino acids 94 to 107 of SEQ ID NO:2; and

(b) a polypeptide consisting of at least amino acids 120 to 127 of SEQ ID NO:2.

58. (Once amended) The isolated polynucleotide of claim 57, wherein said [amino acid sequence] polypeptide is (a).

59. (Once amended) The isolated polynucleotide of claim 57, wherein said [amino acid sequence] polypeptide is (b).

71. (Twice amended) An isolated polynucleotide molecule comprising a nucleic acid 95% or more identical to a reference nucleic acid encoding an amino acid sequence selected from the group consisting of:

(a) amino acids 1 to 127 of SEQ ID NO:2;

(b) amino acids 2 to 127 of SEQ ID NO:2; and

(c) the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97856;

[wherein percent identity is calculated using BESTFIT with the parameters set such that percentage of identity is calculated over the full length of the reference nucleic acid and that gaps in homology of up to 5% of the total number of nucleotide in the reference nucleic acid are allowed] wherein said polynucleotide encodes a polypeptide which binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 127 of SEQ ID NO:2.

72. (Once amended) An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence, wherein, except for one to thirty conservative amino acid substitutions, said amino acid sequence is selected from the group consisting of:

(a) amino acids 1 to 127 of SEQ ID NO:2;

(b) amino acids 2 to 127 of SEQ ID NO:2; and

(c) the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97856 [.];

and wherein said polynucleotide encodes a polypeptide which binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 127 of SEQ ID NO:2.

76. (Once amended) An isolated polynucleotide comprising a nucleic acid encoding an amino acid sequence 95% or more identical to a reference amino acid sequence from the group consisting of:

(a) amino acids 1 to 127 of SEQ ID NO:2;

(b) amino acids 2 to 127 of SEQ ID NO:2; and

(c) the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97856;

[wherein percent identity is calculated using BESTFIT with the parameters set such that percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acids in the reference nucleic acid are allowed] wherein said polynucleotide encodes a polypeptide which binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 127 of SEQ ID NO:2.

77. (Twice amended) An isolated polynucleotide comprising a nucleic acid which is 95% or more identical to a reference nucleic acid, wherein said reference nucleic acid is selected from the group consisting of:

(a) nucleotides 15 to 392 of SEQ ID NO:1; and

(b) nucleotides 12 to 392 of SEQ ID NO:1[;]

[wherein percent identity is calculated using BESTFIT with the parameters set such that percentage of identity is calculated over the full length of the reference nucleic acid and that gaps in homology of up to 5% of the total number of nucleotide in the reference nucleic acid are allowed] and wherein said polynucleotide encodes a polypeptide which binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 127 of SEQ ID NO:2.